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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,449	01/09/2006	Bernd Schwenzer	101215-189	1690

27387 7590 12/20/2006
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EXAMINER	
SHIN, DANA H	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/20/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No: 10/537,449	Applicant(s) SCHWENZER ET AL.	
	Examiner Dana Shin	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-16,19-21 and 23-27* is/are pending in the application.

4a) Of the above claim(s) *13-16,19-21 and 23-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Sequence Rule Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

CFR §1.821(d) reads as follows:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims or the patent application.

Table 2 of the instant application contain nucleic acid sequences which are not preceded by "SEQ ID NO:". Applicants are reminded of the Office communication mailed on June 27, 2006, which specifically and expressly required to make a reference to the sequences by use of the sequence identifiers in accordance with CFR §1.821 through 1.825. See Notice to Comply. Any response to this action must correct this deficiency, as this requirement will not be held in abeyance.

Response to Applicant's Election

Applicant's election with traverse of claims 1-11 (reciting target sequence regions 2206-2225 and 2331-2350) in the reply filed on June 1, 2006 is acknowledged. The traversal is on the ground(s) that the prior art by Cech et al. (US 6,444,650 B1) fails to disclose any special technical features of the instantly claimed invention and that "polynucleotide target sequence regions" are not the subject of the claims and each type of claimed oligonucleotide has identical activity. This is not found persuasive because of the following reasons:

The reference by Cech et al. clearly discloses hTRT (also known as hTERT) antisense oligonucleotides at the first line of the abstract, for example. Moreover, Cech et al. disclose the hTERT sequence recited in the instant claim 1 (see column 3, line 41 & Figure 1). Further, applicants assert that Cech et al. do not disclose antisense oligonucleotides specific to the target sequence regions claimed in the instant case. This is found contradictory to the applicant's own argument that "polynucleotide target sequence regions" are not the subject of the claims while arguing that Cech et al. do not specifically disclose the "polynucleotide target sequence regions". Therefore, per applicant's own argument, the "polynucleotide target sequence regions" should not be used as a factor for determining the presence or lack of contribution over the prior art.

Applicants further argue that oligonucleotides targeting different regions have identical activity. Sharing a common activity, such as antisense activity, is not sufficient to render all claimed alternatives be regarded as being of similar nature because the different target regions have different nucleic acid compositions.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 1-11, 13-16, 19-21, and 23-27 are pending. Claims 13-16, 19-21, 23-27, and DNAzyme, peptide nucleic acid, ribozyme, and siRNA are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Accordingly, claims 1-11 pertinent to an antisense oligonucleotide are currently under examination on the merits.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Note that the certified copies of the foreign papers, 102 58 117.7, 103 06 084.7, and PCT/DE03/04114 are in non-English language and that an English translation has not been filed. Since the examiner cannot determine whether the foreign priority documents provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application, the effective filing date for the instant application will be the filing date of the instant application, January 9, 2006.

Information Disclosure Statement

The listing of references in the Search Report and in the specification is not a proper information disclosure statement. 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored

in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report and in the specification have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Specification

The disclosure is objected to because of the following informalities:

1) The instant disclosure contains drawings, Figures 1-5; however, there is no brief description of the drawings in the specification. See MPEP § 608.01(f). Appropriate correction is required.

2) The abstract of the disclosure is objected to because it contains the word "said". Applicant is reminded of the proper language and format for an abstract of the disclosure, such that the form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. Correction is required. See MPEP § 608.01(b).

3) The instant disclosure contains Table 2 with nucleic acid sequences. It is noted that the nucleic acid sequences are not preceded by SEQ ID NOs. Appropriate correction is required.

This is a second notice concerning sequence non-compliant issues addressed to Table 2. See the Office communication mailed to applicant on June 27, 2006.

Claim Objections

Claims 2, 7, and 9 are objected to for containing non-elected subject matter. Appropriate correction is required.

Claim 9 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 2. Note that both claimed polynucleotides are directed to the hTERT-mRNA sequence. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 9 is further objected to because it recites the "hTERT-mRNA" in line 2, whose acronym has not been positively recited in any of the preceding claims. Inserting the acronym in claim 1 (i.e., the mRNA of the catalytic subunit of human telomerase (hTERT-mRNA)) is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recited GenBank Accession No. AF 015950 in claim 1 is considered to be indefinite because GenBank Accession Nos. may change and thus do not provide constant and unchanging sources of sequence information. Applicant's attention should be directed to the fact that GENBANK information may be updated and revised anytime (see <http://www.ncbi.nih.gov/Genbank/index.html> under the heading Updating or Revising a Sequence), therefore, the claimed sequences could change anytime. In light of the foregoing, one skilled in the art would not be able to ascertain the metes and bounds set forth by the instantly claimed GenBank Accession No and the two regions 2206-2225 and 2331-2350. It is suggested that the GenBank Accession No. be entered as applicant-defined SEQ ID NO.

For examination purpose, the claimed nucleic acid sequence AF 0159550 will be construed to read on SEQ ID NO:18, filed on November 27, 2006. Similarly, the two elected regions 2206-2225 and 2331-2350 will be interpreted to read on SEQ ID NOs:4 and 8, respectively.

Claims 1-2 claim that the polynucleotide "specifically interacts with" the mRNA sequence. It is unclear what is meant by the phrase "specifically interacts with", because neither the claims nor the specification describe what limitations are encompassed by the phrase. For example, one of ordinary skill in the art cannot recognize whether the claimed polynucleotide must hybridize with the target mRNA sequence with 100% identity/homology, or whether 70-80% hybridization meets the requirement of being "specifically" interacted with the target

sequence. Further, the term "interact" is not clearly defined in the instant specification. Note that the term "interact" can be construed to mean a variety of different actions such as recognition, binding, inhibition, cross-linking, and so forth. As such, one of ordinary skill in the art cannot ascertain the metes and bounds set forth by the claim language in the instant case.

Further, claim 1 specifically claims that the polynucleotide interacts with the mRNA in at least two target sequence regions, 2176 to 2250 and 2296 to 2393. It is unclear whether the claimed single polynucleotide must hybridize with the target mRNA in multiple (at least two) regions of the target mRNA simultaneously. If this is what applicant has intended to claim, note that the disclosure of the instant application does not contain any support for a polynucleotide that hybridizes to two or more regions of the target mRNA sequence at the same time. Moreover, it is unclear whether the polynucleotide must interact with the entire length of 2176-2250 (SEQ ID NO:1) as well as that of 2296-2393 (SEQ ID NO:2). For examination purpose, the claimed polynucleotide in the instant application will be construed in light of the instant disclosure: a polynucleotide hybridizing with either region of the hTERT sequence.

Claims 3 and 9 recite the limitation "the sequence region" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim, because claim 1 recites "sequence regions" in a plural form.

Claim 4 specifically claims that the polynucleotide is "immobilized". Although the specification describes that "immobilization is understood to involve various methods and techniques to fix the polynucleotides on specific carriers" (page 7), the metes and bounds

encompassed by the term "immobilized" remains vague and unclear. In particular, the specification discloses a number of different methods (e.g., crosslinking, binding to carrier, inclusion, adsorption, covalent binding, polyacrylamide resins, microencapsulation) on pages 8-9; however, the breadth of the term "immobilization" described in the specification is so broad that one of ordinary skill in the art cannot recognize exactly what is claimed by the claim language "immobilized".

Claim 6 claims that the polynucleotide is "fused" or complexed with "another molecule". It is unclear what is meant by the term "fused" because neither the claim or the specification defines the term. For examination purpose, the term "fused" will be construed to mean "complexed" as claimed in claim 6. Further, the specification does not define what is meant by "another molecule", thus rendering the claim indefinite.

Claims 10-11 claim compositions comprising a polynucleotide and a "pharmaceutically tolerable carrier". Although the specification describes that "the pharmaceutical carrier may comprise additional materials and substances such as medical and/or pharmaceutical-technical adjuvants" (page 9), it remains vague and unclear exactly what is encompassed by the term "pharmaceutically tolerable carrier" because the specification does not further elaborate on the claimed subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is directed to a pharmaceutical composition comprising a polynucleotide specifically interacting with the catalytic subunit of hTERT-mRNA.

Note that this rejection is directed only to the preamble language, "pharmaceutical", and removing the term "pharmaceutical" would be remedial.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Problems related to therapeutic use of nucleic acids were well known in the art at the time of invention. See for example Opalinska et al. (*Nature Reviews Drug Discovery*, 1:503-514, 2002). Such problems include the inability to specifically deliver an effective concentration of a nucleic acid to a target cell, such that a target gene is inhibited to a degree necessary to result in a therapeutic effect.

Opalinska et al. state on page 511

> "[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA"

and in column 2 of the same page,

> "Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded."

Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed methods *in vivo* in all organisms, with a resultant inhibition of hTERT mRNA/protein expression by administering an oligonucleotide targeted to the hTERT mRNA sequence, as claimed. The specification provides *in vitro* cell culture examples wherein hTERT mRNA/protein expression is reduced and growth/proliferation of the cultured cells is inhibited; however, it provides no examples with regard to inhibitory effect of the hTERT antisense oligonucleotides in any *in vivo* experimental system. The prior art by Opalinska et al. teaches that the uptake and biological activity observed *in vitro* would not predictably translate into *in vivo* results due to differences in the physiological conditions of a cell *in vitro* versus *in vivo*. In other words, the instant specification does not provide any working examples with regard to

"pharmaceutical or pharmacological effects" of the instantly claimed invention. Therefore, in the absence of *in vivo* examples in the specification, one of ordinary skill in the art would not know *a priori* whether the hTERT antisense oligonucleotides administered *in vivo* would be delivered to the proper cell in a sufficient concentration and remain for a sufficient time to provide successful inhibition of expression of a target gene, thereby resulting in the claimed "pharmaceutical" effects.

In view of all of the factors listed above and the lack of evidence that the exemplified hTERT antisense oligonucleotides entail any pharmaceutical effect, undue experimentation would be required of the skilled artisan to make the claimed invention commensurate in scope, therefore, claim 10 not enabled.

Claims 3, 6, and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof.

In the instant case, the breadth of claims 3 and 8 embraces any and all modifications and mutations, and that of claim 6 embraces any and all molecules that support transport to the target

site. With regard to chemical modifications, the specification discloses the phosphorothioate modification, incorporation of ribonucleotides and partial terminal modification (page 6); however, it is silent about any hTERT antisense oligonucleotide that is chemically modified. With regard to mutations, although the specification recites the different types of mutations as claimed claim 3 (page 3), it does not disclose any antisense oligonucleotide possessing any of the claimed mutations. The claimed subject matter "another molecule" in claim 6 reads broadly on anything that supports transport, uptake, and distribution of the polynucleotide to a target cell, but the specification does not set forth any species of such molecule nor does it adequately describe what is meant by "another molecule".

As broadly claimed, the specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented what is claimed in claims 3, 6, and 8, especially because it does not describe any species of hTERT antisense oligonucleotide that contains mutations (claim 3) or complexed with another molecule (claim 6) or is chemically modified (claim 8). See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-9 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Monia et al. (US 2002/0045588 A1).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15. Note that even if the translated papers are submitted, this rejection will change to §102(a) rejection.

The claims are drawn to a polynucleotide that specifically interacts with the sequence 2176-2250 or 2296-2393 of SEQ ID NO:18, wherein the polynucleotide contains mutations, immobilized (the polynucleotide is fixed on specific carriers), the polynucleotide is antisense oligonucleotide, complexed with a molecule that supports cellular uptake, modified with phosphorothioate bonds, and a kit comprising the polynucleotide and a pharmaceutical carrier.

Monia et al. teach anti-hTERT oligonucleotides that hybridize with the hTERT mRNA sequence. They teach SEQ ID NO:12 whose 10 consecutive nucleotides "CCAGGGCACG" align with the region of 2308-2318 of SEQ ID NO:18 ("CCATGGGCACG"), wherein the nucleotide "T" is inserted in the instant case. However, one of ordinary skill in the art would acknowledge that this additional "T" corresponds to the "addition" that is claimed in claim 3. Further, Monia et al. teach that the anti-hTERT oligonucleotides can be chemically modified including phosphorothioates (paragraph 0034) and immobilized to a carrier (molecule) that

supports cellular uptake of the oligonucleotides (paragraph 0044). They also teach that the anti-hTERT oligonucleotides can be complexed with a pharmaceutically acceptable carrier and a kit comprising the oligonucleotides and the pharmaceutically acceptable carrier can be prepared (paragraph 0056). Accordingly, all the structural limitations set forth in the claims are taught by Monia et al.

Claims 1-2, 7, and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Bentwich (US 2006/0257851).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

The claims are drawn to a polynucleotide comprising the sequence that hybridizes with either SEQ ID NO:1 (alternatively, SEQ ID NO:4) or SEQ ID NO:2 (alternatively, SEQ ID NO:8). See the claim interpretation stated on pages 7-8 herein.

Bentwich teaches SEQ ID NO:100044 that consists of 32 nucleotides. The 12 consecutive nucleotides "UCCCCCAGGACA" of SEQ ID NO:10044 are equivalent to the 12 consecutive nucleotides "TCCCCCAGGACA" of the instant SEQ ID NO:4. Further, the 19 consecutive nucleotides "GACCCCCUCCCCCAGGACA" of SEQ ID NO:10444 of Bentwich would theoretically interact with or hybridize with the 19 consecutive nucleotides "GACACCATCCCCCAGGACA" of the instant SEQ ID NO:4. The nucleotides that are not identical are underlined. Accordingly, all the structural limitations of the claimed polynucleotide are met by Bentwich.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

JZ TC1600
JANE ZARA, PH.D.
PRIMARY EXAMINER

Application No.: 10/537,449

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 37 CFR §1.821(g). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. §§1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. §§1.821-1.825. Applicants attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a Sequence Listing as required by 37 C.F.R. §1.821(c).
- [ ] 3. A copy of the Sequence Listing in computer readable form has not been submitted as required by 37 C.F.R. §1.821(e).
- [ ] 4. A copy of the Sequence Listing in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. §1.822 and/or 1.823, as indicated on the attached copy of the marked-up Raw Sequence Listing.
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. §1.825(d).
- [ ] 6. The paper copy of the Sequence Listing is not the same as the computer readable from of the Sequence Listing as required by 37 C.F.R. §1.821(e).
- [ ] 7. Other:

Applicant Must Provide:

- [ ] An initial or substitute computer readable form (CRF) copy of the Sequence Listing. (If the unidentified sequences are not provided on the CRF)
- [ ] An initial or substitute paper copy of the Sequence Listing, as well as an amendment directing its entry into the specification. (If the unidentified sequences are not provided in the paper copy)
- [ ] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). (If a new paper and/or CRF are required)

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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